FY06 Clinical Research Network Concepts
DAIDS Response to:

AIDS Research Advisory Committee (5/24/04)
&
OAR *ad hoc* Working Group on Restructuring the NIH-Sponsored AIDS Clinical Trials Networks (5/19/04)

Concepts:

- Leadership for HIV and AIDS Clinical Trials Networks
- Sites for HIV Vaccine, Prevention and Therapeutic Clinical Trials

The following represents the response by the Division of AIDS, NIAID, to key issues and questions arising from the presentation of the aforementioned concepts to the OAR *ad hoc* Working Group on Restructuring the NIH-Sponsored AIDS Clinical Trials Networks (5/19/04) and the AIDS Research Advisory Committee (5/24/04). Due to significant parallels between the issues, questions and principles raised by these two reviews, where appropriate, they have been addressed concurrently.

With this document, the Division of AIDS aims to respond to issues and questions and to provide greater clarity for its rationale and approach. Modifications to the proposed concepts, and related actions, are designed to incorporate the valuable input received.

1. **ARAC #1:** Optimal Strategies for Balancing Fixed Infrastructure Costs, Incremental Per Protocol Costs, and Variable per Case Costs

   OAR *ad hoc* WG Principle 9: DAIDS clinical research funding should support appropriate levels of infrastructure and provide DAIDS-controlled incentives to support the direct costs for the conduct of clinical trials

   DAIDS response: The DAIDS agrees strongly with the goals of balancing infrastructure costs, protocol costs, and incentivized support that are endorsed by ARAC and the OAR *ad hoc* Working Group. These points address the need for both science- and performance-driven allocation of research funds with sufficient flexibility to respond to new opportunities, while at the same time, tying performance to funding. The proposed concepts have been designed to address these issues in several ways. First, by keeping a greater proportion of funds reserved at the network level, DAIDS and its partner ICs will have greater flexibility to incentivize network performance by supplementing networks whose agendas are efficiently and effectively addressing NIH's HIV/AIDS scientific priorities. By not allocating all of the network funds 'up front', DAIDS and its partner ICs will have the capability to shift support to where it's most needed. Similarly, at the site level, core funding support basic clinical trials capacity, with additional funds, from networks, to support the variable and incremental costs of protocols. Performance at all levels (sites, networks and the entire network 'enterprise' will be assessed through a comprehensive evaluation plan with

specific performance parameters and metrics appropriate for each 'level' of the program And, by building into the plan, an increased utilization of external scientific review, DAIDS feels that it has provided a means for ensuring accountability at all three levels of the plan (i.e. sites, individual networks, integrated inter-network structure.)

***Impact on Concept(s) and related actions*:** DAIDS will clarify the language in both the Leadership and Site concepts to define the basis of site funding, and will, in the RFAs, provide guidance for sites in constructing 'core' budgets to support basic clinical trials capacity. DAIDS will work closely with the networks to harmonize the site evaluation process. The primary responsibility for site evaluation will continue to remain with the networks and shall constitute one of the measures on which network leadership shall be evaluated.

2. **ARAC #2:** Minimizing Unnecessary Redundancy in the Support Cores

OAR *ad hoc* WG Principle 7a: Duplication of network core resources should be minimized wherever possible by use of common resources
OAR *ad hoc* WG Principle 7b: Avoidance of redundancy in network missions is desirable

***DAIDS response*:** The DAIDS wholeheartedly agrees that elimination of unnecessary redundancy in network missions and support cores is essential both from the standpoints of inter-network scientific coordination and efficiency of resource utilization. Based on past experience in supporting and managing networks, and external input from a variety of sources, DAIDS aims to achieve a balance between the need for networks to be able to function with sufficient independence to accomplish their missions, and the need to coordinate inter-network resource utilization to enhance collaboration, standardization and economization. DAIDS commitment to these principles is underscored by the fact that rather than waiting until FY06, DAIDS initiated efforts to address these issues in 2003, gathering the current network leadership and stimulating the development of a plan to coordinate several key aspects of network mission and function, including: formation and refinement of research agendas, cross-group leadership, accountability, selection and development of pluripotent international clinical research sites, sharing of laboratory resources and protocols for data comparability and efficiency, common data entry interfaces and common data elements, coordination of specimen management procedures for improved quality and efficiency, sharing and/or standardizing training for common needs, greater inter-network interaction for improved communication, coordinated clinical research product acquisition, distribution and provision, and greater efficiency with all resources overall.

***Impact on Concept(s) and related actions*:** The need for inter-network coordination, resource sharing and efficient use of core resources is addressed extensively in the current versions of both the LG and Site concepts. The resultant RFAs shall contain specific language and guidance to ensure that these issues are addressed in applications, and figure prominently in peer review. LG applicants shall be required to identify a proposed group's strengths in cross-cutting areas and describe how their research plan will interact with other NIAID/NIH-sponsored

HIV/AIDS networks. The plan shall specify the areas in which the applicant group will substantively contribute in addressing specific HIV priorities through shared expertise, resources, and procedures that integrate with and complement the scientific agendas of other NIH-sponsored HIV/AIDS clinical research programs. In addition, following award of successful networks, DAIDS will constitute a Managing Partners Committee, one of whose primary responsibilities shall be to ensure that a sound inter-network coordination plan is finalized and implemented. Together, the network evaluation plan, oversight of the Managing Partners Committee by DAIDS, and rigorous external review, will help ensure that the issues of inter-network redundancy and efficiency are addressed. Furthermore, recognizing that these inter-network coordination efforts themselves shall require support, DAIDS has written these activities into the Statement of Work for its Clinical Research Management Support Contract.

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3. **ARAC #3:** Criteria for Evaluation

OAR *ad hoc* WG Principle 3a: Objective external review of major clinical trials should be routine

***DAIDS response*:** DAIDS agrees that specific evaluation criteria are essential to define the goals and objectives for both leadership groups and sites, and to ensure quality, objective external review of applications. Similarly, ongoing review of clinical trials (including trials in development, and implementation) is important to assure high quality science, scientific coordination and responsiveness to changing needs/opportunities. DAIDS fully endorses the recommendations of both ARAC and the OAR *ad hoc* WG to incorporate expert external review at all appropriate levels. DAIDS also agrees that specialized criteria and expertise may be required in the evaluation of proposals for LG's and/or sites from resource limited settings where, for example, capacity building/expansion may be a focus.

Impact on Concept(s) and related actions: The need for evaluation criteria and objective external review are addressed in the current versions of both the LG and Site concepts. As recommended by ARAC and the OAR *ad hoc* WG, DAIDS and partner IC's, in conjunction with NIAID's Scientific Review Program, will develop evaluation criteria for the LG and site RFAs, that define the priorities, goals and objectives and clarify the areas of emphasis. Furthermore, NIAID and its IC partners recognize the need for a fair and open competition for all LG and Site applicants, including new applicants from rural sites, clinics, resource limited settings, etc. We shall work to ensure that appropriate evaluation criteria are developed and implemented, and that peer-review groups are constituted with the requisite expertise to provide informed assessment of all applications.

4. **ARAC #4:** Clinical Management Support Contract

***DAIDS Response*:** DAIDS agrees with ARAC's assessment of this support contract. DAIDS also agrees that their exists a commensurate requirement for appropriate technical and administrative personnel to make effective and efficient

use of this resource to provide services not routinely available as part of networks or other clinical research projects.

Impact on Concept(s) and related actions:

The need for appropriate staffing and management of DAIDS Clinical Research Management Support Contract is currently being addressed through an analysis of anticipated contract activities, staff expertise and workload impact. A staffing plan for a cross-DAIDS team to manage the contract is under development. Since the CRMS contract is the product of a separate initiative, and the focus of the input is focused on DAIDS management, no modification to the LG or Site concepts is planned.

5. **ARAC #5**: Effective Partnerships at NIH

OAR *ad hoc* WG Principle 6: To provide better coordination and efficiency and avoid redundancy, strong incentives should be given for intra-country communications and collaboration between all similar resources (i.e., reference labs, research support contracts, community input, etc. supported by NIH [all Institutes, Centers and Divisions], but also by CDC, EU/EDCTP, ANRS, MRC, WHO, philanthropy, etc.). Promotion of local or in-country scientific and administrative leadership, ownership and investment in the research enterprise could also promote improved coordination and efficiency.

OAR Response: OAR will endeavor to ensure that other ICs evaluate and identifying their role and the degree to which they shall support specific research activities covered in the RFAs. OAR has clearly indicated that it shall not mandate the participation of and/or commitment of resources from other ICs.

DAIDS Response: DAIDS agrees strongly with the recommendation to coordinate with other NIH ICs as well as other agencies, governments, foundations, charitable organizations, etc. With respect to NIH ICs, since DAIDS cannot control or be responsible for the commitment of other ICs, it is hoped that this would not be a deciding factor in the approval of these concepts.

Impact on Concept(s) and related actions: DAIDS has actively engaged NICHD, NHLBI, NIDA, NIMH, NIDCR, NIDDK, NIAAA, NCRR, NCCAM, NCMHHD and NINR, in order to identify collaborative research opportunities and, where possible, obtain funding commitments. IC-specific priorities are being incorporated into the scientific priority areas of the developing RFAs, and this process shall continue in an ongoing fashion. Significant effort is also being devoted to planning for representation in network activities and governance, to appropriately reflect commitment, roles and responsibilities of IC partners. DAIDS is also working closely with the NIAID Division of Microbiology & Infectious Diseases to develop opportunities for collaboration particularly around areas of co-infections associated with HIV/AIDS.

6. **ARAC #6**: Effective Partnerships with Other Agencies

OAR *ad hoc* WG Principle 6: To provide better coordination and efficiency and avoid redundancy, strong incentives should be given for intra-country communications and collaboration between all similar resources (i.e., reference labs, research support contracts, community input, etc. supported by NIH [all Institutes, Centers and Divisions], but also by CDC, EU/EDCTP, ANRS, MRC, WHO, philanthropy, etc.). Promotion of local or in-country scientific and administrative leadership, ownership and investment in the research enterprise could also promote improved coordination and efficiency.

DAIDS Response: DAIDS strongly concurs with the recommendation to form effective partnerships with other agencies and shall, to the extent possible, support these goals. Many of the very worthy and important activities recommended are, however, beyond the scope of DAIDS to enact. As such, it is hoped that achievement of these goals will not be a deciding factor in the approval of these concepts.

Impact on Concept(s) and related actions: DAIDS has formed linkages and has developed (or is developing) collaborative plans with US Government agencies, including DOD, CDC, State, USAID & HRSA, to maximize the opportunities to link our research programs with HIV/AIDS efforts in those organizations. DAIDS has also reached out to EDCTP, MRC, ANRS, World Bank, BMGF, FNIH, a variety of NGO's, and other organizations with complementary strengths and shared interests. For example, in conjunction with the NIAID's Office for Global Affairs and DMID, plans are underway the EDCTP to coordinate site capacity building and expansion in several locations where both the EC and NIH have research interests and investments in HIV/AIDS, TB and malaria research. DAIDS and ANRS are in active collaboration around the role for cohort studies and biometrics in assessing trends in the global pandemic to better inform prevention and treatment intervention studies. DAIDS has also been collaborating with World Bank to develop an effective and sustainable model for partnership between the two agencies, in conjunction with WB-supported countries to: a) leverage the expertise and resources of both agencies and selected countries; b) leverage the WB Multi-Country HIV/AIDS Program (MAP) funds and possibly other Bank programs; c) to define country contribution on a case-by-case basis. These and other ongoing activities speak to DAIDS commitment to this important goal of inter-agency coordination articulated by ARAC and the OAR *ad hoc* WG.

7. **ARAC #7:** Role of Major Interdisciplinary Centers vs. Smaller Clinical Sites

DAIDS Response: DAIDS agrees with the ARAC with respect to the different, but important roles that smaller clinical sites can play in HIV/AIDS research. One of the major innovations in the proposed concepts, based on input gathered from several sectors, is the increased opportunity (and flexibility) for these kinds of sites to become involved in the future networks, contributing in ways that maximize their strengths. Virtually any type of site (e.g. small, large, urban, rural, single-focus, multidisciplinary, etc.) that can contribute substantially to a group (or groups') research agenda, can apply (or be part of an application) for site

funding, and attain affiliation with a network(s). Flexible application options which may enhance involvement of such sites include partnerships with single or multiple sites (e.g. in-country, North-South, South-South) with complementary scientific, operational, administrative strengths.

Impact on Concept(s) and related actions The flexible application/funding options for small clinical sites are an innovation of this concept that may not be widely known or appreciated. To address this, DAIDS will clarify and highlight these opportunities in the RFA. In addition, based on prior experience with complex solicitations, DAIDS has learned the value of, and will conduct a series of pre-application meetings (shortly after the RFA release) in a variety of locations worldwide, including resource poor settings and rural areas, domestically and internationally. DAIDS will also produce and distribute information and guidance to prospective applicants and be available to respond to questions, in an ongoing manner.

8. **ARAC #8:** Clinical and Basic Science Research vs. Clinical Trials Research

DAIDS Response: Basic research is not one of the priority research areas encompassed in this solicitation and DAIDS is not seeking to support it through this initiative. Nonetheless, there is a great deal of applied research that has come out of the networks to date, and DAIDS would want to see that continue.

Impact on Concept(s) and related actions: DAIDS will include language in the RFA to indicate that basic research is not a scientific priority and will not be directly supported through the network programs.

9. **ARAC #9:** Definition of "Optimizing Clinical Management"

DAIDS Response: DAIDS agrees that it is important to clearly define this area of scientific priority in the proposed concepts. A primary aim of this area of emphasis is to evaluate the effectiveness of new regimens, particularly those that incorporate agents with novel mechanisms of action or new treatment strategies. It is anticipated that trials will be conducted which look at new combinations of treatment modalities incorporating single or multiple new agents with the aim of choosing those which provide improved outcomes on the basis of safety, adherence, delay or elimination of the development of resistance, durability of response and prevention of transmission. A major focus will also be on concurrent evaluation of the impact of ARV and other therapeutic modalities on the management of co-morbidities and co-infections. Optimization of clinical management clearly includes aspects of applied clinical research such as studies evaluating use of agents currently available in better ways – e.g. comparison of regimen employing drugs which can be used for once vs. twice daily dosing, studies evaluating the timing of initiation of ARV therapy coincident with or after TB therapy, clinical and virologic outcomes when therapy is delivered in clinic setting or under direct observation in home based care, studies of the impact of traditional medicines on response to therapy. Participation of other NIH institutes as well as other federal agencies and international partners (e.g. DoD, EDCTP,

WHO, CDC, World Bank and others) will be essential in carrying out these aspects of the scientific agenda.

Impact on Concept(s) and related actions: In order to more clearly convey the intent of this priority area, DAIDS will change its name to: "Optimization of Clinical Management, Including Co-Morbidities". The RFA will provide detailed example of the types of research that distinguish this area from more traditional 'drug development' and clarify its relationship to "operational research" in order to elucidate those areas in which NIH-supported biomedical research can best contribute to improved care and treatment of HIV/AIDS.

10. **ARAC # 10:** Prevention Research

    OAR *ad hoc* WG Principle 2: DAIDS scientific priorities for AIDS clinical research in the areas of therapeutics, vaccines, and prevention should be more clearly defined now, be integrated with and reflect the priorities and plans of other NIH HIV/AIDS research endeavors, and be reassessed annually

    DAIDS Response: DAIDS agrees that each area of scientific priority (including prevention research) requires greater definition than the concept format permits. DAIDS presentation to ARAC (May 2004) detailed the content, goals and objectives of each scientific priority area, including integration and prioritization with other NIH ICs. NIAID's focus in prevention research is centered in biomedical interventions. It is critical that biomedical-based prevention research be tightly linked with behavioral research.

    Impact on Concept(s) and related actions: DAIDS will, in the RFAs, clearly define and provide examples for each priority area of research, including those aspects of prevention research with are outside of HIV vaccines, mother-to-child transmission, and microbicides (e.g. STI treatment, ARVs, male circumcision research, behavioral research). DAIDS will also continue its ongoing efforts to collaborate with NIH ICs with complementary strengths (e.g. behavioral research, special populations) to foster a comprehensive approach to HIV prevention research.

11. **ARAC #11**: Highest Priority Science Should Drive the Structure (i.e., Infrastructure) of the NIAID Clinical Trials Endeavor, rather than Visa Versa

    OAR *ad hoc* WG Principle 1: The highest priority science must drive the structure of NIAID's clinical trials endeavor, rather than vice-versa

    DAIDS Response: DAIDS agrees that networks ('one mechanism') cannot meet all of the clinical HIV/AIDS research needs. DAIDS concurs with ARAC and the OAR *ad hoc* WG that NIAID should support a portfolio of HIV/AIDS clinical research capabilities which collectively have the expertise and means to address all of the highest priority scientific areas and questions. In this context, DAIDS believes that networks have an important role. The proposed LG and Site

concepts and resultant RFAs are designed to address the network component of DAIDS HIV/AIDS clinical research portfolio.

DAIDS believes that the role for networks is based on their strengths. By bringing expert investigators together in collaborative groups, networks can provide a rigorous scientific environment in which peer-review sharpens ideas and leads to high quality research. Networks provide continuity for strategic planning and product development and offer re-usable infrastructure which can promote not only efficiency, but improved data quality and comparability – all very desirable features of a clinical research endeavor. At the same time, networks have their weaknesses (e.g. protocol development can be slow, networks can be overly risk averse or dogmatic, 'science by committee' can reduce creativity, networks can function in isolation from one another). Moreover, DAIDS networks of the past, with few exceptions, have not been very well 'tooled' to address some of the kinds questions that now figure prominently and shall require new/different thinking, strategies and resources. The present concepts represent DAIDS' efforts to form networks that are better-suited to carrying out the types of research that are required, retaining and optimizing that which networks do best, and fixing (or eliminating) what is broken. DAIDS has clearly delineated its expectations for inter-network scientific and logistical leadership and coordination in several key areas (e.g. site and laboratory selection and development, data management, protocol development, training, acquisition and distribution of clinical research products, inter-network communication and overall efficiency). To ensure that these important aspects are addressed, DAIDS will place major responsibility on network leadership (Managing Partners Committee) while providing needed support (Clinical Research Management Support contract) for these activities. To enhance accountability, DAIDS shall enact a multi-level performance evaluation plan incorporating substantial objective external review, and this shall be linked to funding at both the site and network levels. Taken together, DAIDS believes that its approach embodies the vision as well as the specific elements required to stimulate the formation of networks designed and constructed and managed in ways that will promote first-rate coordinated research that addresses the scientific priority areas, with rigor and efficiency, and thereby maximizes the important capabilities that networks can provide.

At the same time, DAIDS has always and shall continue to support 'non-network' research mechanisms to address HIV/AIDS clinical research questions. Currently, DAIDS supports a variety of investigator-initiated trials ranging from single-site studies to large multi-national projects, across the spectrum of vaccine, prevention and treatment both in the US and internationally (including developing countries). Included are studies of ARVs (adult and pediatric, regimens, adherence, resistance), immune-based therapies (IL-2, cellular therapies), HIV vaccines, interventions of mother-to-child transmission, male circumcision, co-infections (including STI, TB, HCV) and behavioral interventions. DAIDS also recognizes and shall continue to support an important role for observational databases (domestic and international). A joint initiative with OAR (International Databases to Evaluate AIDS) will link US, European, and other datasets to help assess global trends in the HIV/AIDS epidemic and inform strategic planning of

international clinical trials. To further support our continued commitment to non-network research, DAIDS has led a trans-NIAID effort to redesign the process by which investigator-initiated trials can be submitted and funded. The new process will facilitate rapid review of trial concepts, provide support for protocol development and preparedness, and expedite award of cooperative agreements for study implementation.

In addition, DAIDS (as it has in the past) shall continue to utilize a variety of mechanisms to support HIV/AIDS clinical research that may not be well-suited to investigation in networks. Focused areas (and types) of research that are beyond the capabilities/strengths of networks (or underrepresented therein) can be identified and, through the NIAID initiative process (including ARAC review), be addressed through the issuance of Program Announcements, Requests for Applications, Requests for Proposals, etc. designed specifically to meet the particular research need(s). DAIDS has and will continue to rely on such mechanisms to advance research in areas such as acute infection and early disease, vaccine, microbicide and therapeutics design and development, HIV co-infections, others) and is always open to input on how to best match its research portfolio with the highest priority needs. The funding of networks will not preclude the use of these, and other 'non-network' mechanisms for supporting high priority clinical HIV/AIDS research.

Impact on Concept(s) and related actions: DAIDS shall work diligently to ensure that networks address the highest priority research questions that are well-suited to investigation in that setting. At the same time, DAIDS shall remain receptive and responsive to input and suggestions for the use of 'non-network' mechanisms to address research that is under-represented or not optimally-suited for study in networks.

12. **ARAC #12**: Annual Reassessment of Scientific Priorities for Clinical Trial Research.
ARAC #13: Regular External Evaluation of Network Progress.

OAR *ad hoc* WG Principle 3b: Regular external evaluation of the progress of the standing networks should be conducted and that oversight should be integrated into network operations**.**

DAIDS Response: DAIDS agrees that regular external evaluation of the agendas, scientific priorities, and progress of networks should be a key component of the oversight, evaluation and management plan. In the past, DAIDS has convened external reviews of networks for oversight and planning purposes; such reviews have been instrumental in guiding mid-course corrections and strategic future planning. DAIDS agrees that ARAC (including *ad hoc* subject matter experts as needed), and ARAC working Groups (e.g. AIDS Vaccine Research Working Group), could be well-suited to conduct regular assessments of network priorities and progress, and that such evaluations could be the basis for informed recommendations linked to the OAR Plan for HIV-Related Research.

Impact on Concept(s) and related actions: DAIDS will work with ARAC to determine how best to design and implement the types of objective, external review that is jointly endorsed. The January ARAC meeting, most often used to discuss research priorities and plans as a foundation for the review of upcoming initiatives, may be an optimal time to schedule this activity.

13. **ARAC #14**: Objective External Review and Approval of Major (e.g., Expensive) Clinical Trials

    OAR *ad hoc* WG Principle 3a: Objective external review of major clinical trials should be routine

    DAIDS Response: DAIDS agrees with the need for external review of plans for, and progress of major clinical trials. DAIDS will work closely with network leadership to identify, at an early stage, plans for large and/or high resource studies in order that DAIDS can initiate appropriate external review. Such review can identify and evaluate resource requirements (monetary, volunteers, sites, etc.), including potential impact on other programs; this kind of input can be critical in identifying opportunities to coordinate with other programs/agencies, etc.

    Impact on Concept(s) and related actions: DAIDS will work with ARAC to determine how best to design and implement the objective external review of major clinical trials.

14. **ARAC #15**: Streamlining Protocol Development

    OAR *ad hoc* Working Principle 5: Protocol development and implementation must be streamlined and be appropriate for the science being conducted

    DAIDS Response: DAIDS agrees that network protocol development should be streamlined and more efficient, and embraces the suggestions to invoke project management teams, sufficiently resourced, to expedite protocol development.

    Impact on Concept(s) and related actions: DAIDS will, in the RFAs, emphasize the need for efficiency in protocol development. Protocol development procedures and management will be included in the review criteria used to evaluate network applications. Furthermore, where relevant, DAIDS will invoke industry-based (or other relevant) standards of performance against which networks will be evaluated.

15. **OAR *ad hoc* Working Group Principle 4**: Community involvement and participation must be routinely incorporated into all components of DAIDS-supported clinical research and supported through specific mechanisms with investment of resources

    DAIDS Response: DAIDS is in full agreement with the need to include community input at all levels of network functioning. DAIDS will continue to

require community input at the site and network levels. In addition, DAIDS has proposed formation of a Community Partners Committee to enhance intra- and inter-network community input, identify and develop programs to meet training and support requirements, increase community input and participation in resource poor settings, address challenges to participation (economic, cultural, language, history, etc.), and enhance the activities of community advisory boards.

Impact on Concept(s) and related actions: The need for inclusion of community input at all levels is addressed in the current versions of both the LG and Site concepts and shall be strongly represented in the RFAs. Discussions are actively ongoing between DAIDS, community representatives, community advisory boards, and current network leadership to further identify issues of relevance, and to formulate the role, membership and structure of the Community Partners Committee.

16. **OAR *ad hoc* Working Group Principle 8**: Training and capacity building that promotes local or in-country ownership/investment in the research enterprise must accompany research support for sites in both U.S. and international resource-poor settings

DAIDS Response: DAIDS is in full agreement with the need for training and capacity building in resource-poor settings (in the US and internationally) to ensure durable and sustainable clinical research capability. DAIDS proposes to address these requirements through a matrix of support and capacity-building mechanisms. Direct interactions with in-country investigators have made clear that a key component of successful scientific capacity-building is found in inter-site partnerships; as such, DAIDS has enhanced these opportunities in both Site and LG concepts. The site concept provides considerable flexibility to tailor flexible inter-site linkages, while the LG concept, through the establishment of a Managing Partners Committee, links network leadership in a strategic partnership to assess, plan and implement training and capacity-building activities across the entire network enterprise. DAIDS also recognizes the need to support capacity-building in several areas that may fall outside (or stretch the capabilities of) partner academic institutions, such as assistance with research program management, recruiting, staffing, data management, financial management, training, translation, and community input enhancement. This support must be stable and durable in order to ensure long-term site development. As such DAIDS has designed its Clinical Research Management Support contract as a versatile resource to assist sites and networks in providing these (and other) support services required to build and help maintain clinical research capacity. And, by continuing and expanding linkages with other NIAID (e.g. CFAR, CIPRA), Fogarty Center (e.g. AITRP, ICOHRTA) and other agency (e.g. EDCTP, World Bank, BMGF) programs, DAIDS will continue to address the important needs for broad-based training and capacity-building that are essential for sustainable research capability.

Impact on Concept(s) and related actions: To better respond to the needs for training and capacity-building, DAIDS has modified its original concepts, merging what were formerly two separate Domestic and International Site

concepts, into a single Clinical Site concept. DAIDS' rationale for this modification is to provide greater opportunities for sites with complementary interests/capabilities to form a variety of flexible linkages to meet specific needs. Cognizant of the differing capacities and requirements of sites in resource poor (vs. capitalized) settings, NIAID will correspondingly design and incorporate suitable review criteria and peer-review committees to fairly, yet rigorously review applications. To ensure that the Managing Partners Committee provides strategic leadership in training and capacity-building, and efficient use of resources, DAIDS, in conjunction with external review, shall evaluate the quality, timeliness and effectiveness of coordinated capacity building activities across networks and make modifications as needed.